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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,326	03/20/2006	John Nicholas Staniforth	478.1073	8789

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
10/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,326	STANIFORTH ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 6-9, 14-31, 33-37, and 39-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-9, 14-31, 33-37, and 39-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-9, 14-31, 33-37, and 39-40 are pending. Applicants amended claims 1, 3, and 20-21. Applicants previously cancelled claims 5 and 10-13. Applicants newly cancelled claims 32 and 38. Receipt and consideration of Applicants' amended claim set, amended specification, and remarks/arguments submitted on July 12, 2010 are acknowledged. All rejections/objections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments and/or persuasive arguments.

Election/Restrictions

The species election **is maintained** at this time.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Applicant is granted benefit of the foreign priority document GB 0231612.4 with a filing date of September 15, 2003.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-9, 15-31, 33-37, 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards et al. (US 2002/0035993) in view of the 1993 Drug Information Handbook (Lacy, C. et al., Lexi-Comp, Inc.: Cleveland, 1993, pp 506-507) ("DIH"), Gupta et al. (US 2002/0006933), Merkus (U.S. Patent No. 5,942,251) and Keller et al. (U.S. Patent No. 6,645,466).

Applicant Claims

Applicants claim a passive dry powder inhaler (passive DPI) device containing a dry powder formulation comprising apomorphine and a metal stearate, wherein upon actuation of the device a dosing efficiency at 5 microns of at least 70% is achieved.

NOTE: The recited product-by-process limitations recited in Applicants' dependent claims 4, 6-9, and 39-40 are noted, but are not deemed to result in a material structural property of the recited dry powder contained in the claimed passive DPIs.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Edwards teaches inhalable dry powder compositions characterized by **a tap density less than 0.4 g/cc, a mass median aerodynamic diameter (i.e. particle size) ranging from about 1 micron to about 5 microns, and a delivery efficiency of at least 50% that are suitable for administration from single breath-actuated inhalers** (i.e. passive dry powder inhalers) (abstract; ; [0018]; [0022]-[0024]). A variety of active agents may be incorporated into the inhalable particles, such as **L-Dopa**, etc. ([0024], [0055]-[0057]; Example 5: [0199]-[0203]). The inhalable particles are made **by spray drying** ([0158]-[[0172]). Suitable commercially available passive DPIs are disclosed in [0080].

The DIH establishes that **L-Dopa is used to treat Parkinson's disease** (pp 506).

Gupta teaches that **apomorphine is suitable for the treatment of Parkinson's disease and has been administered by inhalation administration via the nose** [0041]-[0044]. Gupta teaches **inhalable apomorphine powder formulations** (abstract; [0021]; [0027]; [0047]).

Merkus teaches that **apomorphine aqueous formulations are unstable**, implying that apomorphine is sensitive to moisture (col. 4, lines 16-17).

Keller teaches inhalable dry powder formulations, wherein the inclusion of magnesium stearate improves the resistance of the active agents contained in the inhalable dry powders to moisture (abstract; col. 4, lines 55-67; col. 45, lines 49-52; col. 6, lines 38-51).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Edwards lacks the teaching of passive dry powder inhalers containing pharmaceutical formulations comprising apomorphine and a metal stearate. These deficiencies are cured by the teachings of Gupta and Keller.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious to a person of ordinary skill at the time of the instant invention to modify Edwards exemplified L-Dopa formulations to obtain formulations comprising apomorphine, because both L-Dopa and apomorphine are known to be suitable for the treatment of Parkinson's disease (Gupta and Edwards) and both have been known to be formulated in inhalable dry powder formulations (Gupta and Edwards). An ordinary skilled artisan would have been motivated to include magnesium stearate in Edwards formulations modified to contain apomorphine, because apomorphine is known to be unstable in the presence of water (Merkus) and magnesium stearate is known to improve the resistance of water-sensitive active agents in inhalable dry powder formulations (Keller). An ordinary skilled artisan would

have had a reasonable expectation of combining the teachings of Edwards, Gupta, and Keller, because all these references teach inhalable dry powder formulations and the incorporation of magnesium stearate is known in inhalable dry powder formulations. Furthermore, an ordinary skilled artisan would have been motivated to substitute L-Dopa for apomorphine with a a reasonable expectation of success, because both compounds are known to be suitable for treatment of Parkinson's disease and Edwards explicitly teaches that a wide variety may be incorporated into the inhalable particles.

Regarding the reciting dosing efficiencies, Edwards teaches overlapping efficiencies. A prima facie case of obviousness necessarily exists when the prior art range overlaps or touches a claimed range, such as in the instant rejection. MPEP § 2144.05. Similarly, the prior art teaches overlapping tap density values compared to the tap densities recited in claims 34-35 of the instant application. Regarding a tap density range of 0.5 g/cc or greater, it is the Examiner's position that dry powders having a tap density of about 0.4 g/cc as taught by Edwards would be reasonably expected to exhibit similar properties compared to dry powders having a tap density at the lower end of the recited tap density range in dependent claim 36 of the instant application (e.g. tap densities of ~0.50 g/cc would be expected to behave similarly to particle having a tap density of ~0.40 g/cc, such as 0.39 g/cc). Regarding the properties recited in Applicants' dependent claims (e.g. producing a peak blood plasma level within 1-20 minutes of pulmonary inhalation), these properties are considered to necessarily result from the inhalation administration of apomorphine dry powders. Because the aforementioned prior art formulations fairly suggest inhalable apomorphine dry powders comprising a metal stearate and the inhalation administration of these powders, it is concluded that practice of the prior art teachings would

necessarily result in the same recited properties. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments with respect to claims 1-4, 6-9, 15-31, 33-37, 39-40 have been considered but are moot in view of the new ground(s) of rejection.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards et al. (US 2002/0035993) in view of the 1993 Drug Information Handbook (Lacy, C. et al., Lexi-Comp, Inc.: Cleveland, 1993, pp 506-507) ("DIH"), Gupta et al. (US 2002/0006933), Merkus (U.S. Patent No. 5,942,251) and Keller et al. (U.S. Patent No. 6,645,466) as applied to claims 1-4, 6-9, 15-31, 33-37, 39-40 above, and further in view of Licalsi et al. (U.S. Patent No. 6,651,655).

Applicant Claims

Applicants claim a passive dry powder inhaler (passive DPI) as described above, wherein the dry powder formulation is pre-metered in one or more foil blisters.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Edwards, the DIH, Gupta, Merkus, and Keller are set forth above.

Licalsi establishes that **foil blisters are conventionally used in the art with multidose dry powder inhalers** to facilitate the delivery of many doses (col. 4, lines 30-32).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Edwards lacks the teaching of a passive DPI with a dry powder formulation pre-metered in foil blisters. This deficiency is cured by the teachings of Licalsi.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious to a person of ordinary skill at the time of the instant invention to pre-meter doses of a dry powder to be delivered from a DPI in foil blisters, because it is a conventional practice in the art to utilize pre-metered dry powder formulations contained in foil blisters with multidose dry powder inhalers. An ordinary skilled artisan would have been motivated to use foil blisters to contain pre-metered inhalable dry powder formulations for use with a dry powder inhaler and would have had a reasonable expectation of doing so, because foil blisters are conventionally used in the prior art for this purpose (Licalsi). Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments with respect to claim 14 have been considered but are moot in view of the new ground(s) of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 19-31 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 21, 24, 26, 42, and 44 of copending Application No. 10/552,231 (copending '231). Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets recite or claim apomorphine compositions comprising apomorphine and a metal stearate. Independent claim 1 of the instant application is described above. Dependent claim 26 of copending '231 claims a composition for pulmonary inhalation comprising (i) apomorphine in an amount to provide a nominal dose of from about 100 to about 1600 micrograms of apomorphine and (ii) from about 0.15% w/w to about 5% w/w of an additive selected from a group consisting

of leucine, magnesium stearate, lecithin, and sodium stearyl fumarate. Both magnesium stearate and sodium stearyl fumarate are metal stearates.

The primary difference between dependent claim 26 of copending '231 and the claims of the instant application is that dependent claim 26 of copending '231 does not recite that the composition is contained within a passive dry powder inhaler (i.e. a breath-actuated DPI) or that the apomorphine composition has a dosing efficiency at 5 microns of at least 70%. Dependent claims 21 and 24 of copending '231 establish that it is an obvious modification of the claimed composition of copending '231 to formulate the composition where the apomorphine is in the form of particles having a MMAD of 5 microns or less. It is the Examiner's position that the apomorphine particulate composition comprising apomorphine and a metal stearate and having a MMAD of 5 microns or less would necessarily exhibit the recited dosing efficiency. Dependent claims 42 and 44 of copending '231 establish that an obvious modification of the claims of copending '231 would be to place said compositions within a passive DPI (i.e. a breath-actuated inhaler device). Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-4 and 6-7 *prima facie* obvious claims 1, 21, 24, 26, 42, and 44 of copending Application No. 10/552,231 (copending '231).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants arguments/remarks submitted on July 12, 2010 did not traverse the instant rejection and indicated that Applicants would consider filing a terminal disclaimer upon the identification of allowable subject matter. The instant rejection is maintained.

Claims 1-4 and 19-31 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 99-100 of copending Application No. 12/459,686 (copending '686) in view of Staniforth et al. (US 2004/0204439).

Independent claim 1 of the instant application is described above. Dependent claim 100 of copending '686 claims a composition for pulmonary inhalation comprising (i) apomorphine in an amount to provide a nominal dose of from about 100 to about 600 micrograms of apomorphine, (ii) from about 0.1% w/w to about 10% w/w of a carrier material, and (iii) a force control agent selected from a group consisting of leucine, magnesium stearate, lecithin, and sodium stearyl fumarate. Both magnesium stearate and sodium stearyl fumarate are metal stearates.

The primary difference between dependent claim 100 of copending '686 and the claims of the instant application is that dependent claim 100 of copending '686 does not recite that the composition is contained within a passive dry powder inhaler (i.e. a breath-actuated DPI) or that the apomorphine composition has a dosing efficiency at 5 microns of at least 70%. These deficiencies are cured by the teachings of Staniforth set forth above. Thus, it would be a prima facie obvious modification of claim 100 of copending '686 in view of the teachings of Staniforth

to place the composition of claim 100 of copending '686 within a passive dry powder inhaler and to use particulate apomorphine having a dosing efficiency at 5 microns of at least 70%. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-4 and 19-32 *prima facie* obvious claims 1, 21, 24, 26, 42, and 44 of copending Application No. 10/552,231 (copending '231).

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

Applicants arguments/remarks submitted on July 12, 2010 did not traverse the instant rejection and indicated that Applicants would consider filing a terminal disclaimer upon the identification of allowable subject matter. The instant rejection is maintained.

Conclusion

Claims 1-4, 6-9, 14-31, 33-37, and 39-40 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, ~10:00-6:00 and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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